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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,955	09/28/2001	Juan J. Perez-Villar	D0029 NP	4833

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EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,955	PEREZ-VILLAR ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 36-69 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/17/02, 9/18/02,*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *4/11/06*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-10, 14-15, 34,) in the reply filed on 6/21/2006 is acknowledged. Claims 1-35 have been canceled (6/21/2006).

All pending new claims 36-69 corresponding to the elected invention are under consideration by the Examiner.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title of the invention be amended to recite "A nucleic acid encoding human Clnk-related gene, MIST (Mast Cell Immunoreceptor Signal Transducer)".

Claim rejections-35 USC § 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make use the invention.

The deposit of biological material is considered by the Examiner to be necessary for the enablement of the current invention because the claims require availability of the deposit. Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological

material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC §112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining ATCC Deposit No. PTA-736 and it does not appear to be a readily available material. The ATCC® PTA-2981 deposit in full compliance with 37 CFR §§ 1.803-1.809 would satisfy the requirements of 35 USC §112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In the instant case, Applicants have made a deposit of PTA-2981. However, the statement submitted on 6/21/2006 fails to recite that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent".

A new statement reciting all the necessary criteria stated above is required to satisfy the deposit requirements. See 37 CFR 1.808.

3b. Claims 47-48, 65-69, are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid having at least 95% sequence identity with a particular disclosed sequence (SEQ ID NO:1). The claims do not require that the polypeptide encoded by the nucleic acid possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids encoding

polypeptides that is defined only by sequence identity. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved for the biological activity of the polypeptide that binds Grb2, Vav, Lat, c-Cbl or SLP-76. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics and structure/function relationship, the specification does not provide adequate written description of the claimed genus of nucleic acid molecules. Similarly, the specification does not provide an adequate written description for a polynucleotide containing a single nucleotide substitution, which substitution can be in a conserved or a non-conserved nucleotide resulting in an amino acid substitution in the polypeptide of amino acid sequence set forth in SEQ ID NO:2.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the ad that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the written description' inquiry, whatever is *now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acid molecules encoding polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the

complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only a nucleic acid encoding a polypeptide of amino acid sequence set forth in SEQ ID NO:2 as recited in claim 36, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

3b. Claims 47-48, 65-69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide of amino acid sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for an isolated nucleic acid having at least 95% sequence identity with a particular disclosed sequence (SEQ ID NO:1) wherein the polypeptide binds Grb2, Vav, Lat, c-Cbl or SLP-76. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 47, for example, is overly broad in its limitation of "at least 95% sequence identity" because no guidance is provided as to which of the myriad of nucleic acid molecules encompassed by the claim will encode a polypeptide which retains the characteristics of the

desired polypeptide binds Grb2, Vav, Lat, c-Cbl or SLP-76. Variants of a nucleic acid can be generated by deletions, insertions, and substitutions of nucleotides, but no actual or prophetic examples on expected performance parameters of any of the possible variants of the claimed nucleic acid molecule or muteins of the protein molecule have been disclosed. Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate and use a nucleic acid having at least 95% sequence identity with SEQ ID NO:1 (the encoded polypeptide having the biological activity of binding to Grb2, Vav, Lat, c-Cbl or SLP-76.), other than the polynucleotide of SEQ ID NO:1 exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any

experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of the claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim rejections-35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 52 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 52 is rejected as vague and indefinite because it recites "polynucleotide which represents the complete complementary sequence of (a) or (b) of Claim 36." It is unclear how the complementary nucleic acid can encode a polypeptide of amino acid sequence set forth in

SEQ ID NO:2. It is suggested that a claim encompassing a complete complementary sequence of SEQ ID No:1 be written as an independent claim.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5a. Claims 36-43, 47-69, are rejected under 35 U.S.C. 103(a) as unpatentable over Goitsuka et al (April 2000).

Goitsuka et al describes a partial isolated human MIST cDNA (see Methods, cDNA cloning and expression constructs, Figure 1). A copy of the comparison of SEQ ID NO:2 presented in the instant invention and the human MIST amino acid sequence disclosed in the reference is enclosed at the end of this action (SEQUENCE COMPARISON A). However, Goitsuka does not disclose the complete nucleic acid encoding the protein set forth in SEQ ID

NO:2. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant invention was made to use the cDNA disclosed by Goitsuka to screen a human cDNA library of human cord blood-derived mast cells to obtain the complete cDNA encoding human MIST and place the cDNA encoding human MIST, in an expression vector and host cell which expresses the putative protein encoded thereby, and recovering the recombinant protein produced. To have incorporated the recombinant DNA encoding the protein identified as human MIST by Goitsuka et al, into an expression vector and host cell to facilitate the production and characterization of the MIST protein encoded thereby by employing those methods that were old and well known in the art of molecular biology at the time that the instant invention was made would have been *prima facie* obvious to an artisan in light of the Goitsuka publication. Furthermore, it would have been obvious to one of ordinary skill in the art at the time that the invention was made, to make fragments of the cDNA encoding fragments of the human MIST protein as well as to make single nucleic acid substitutions in the human MIST cDNA to determine the relevance of the amino acids with respect to the biological activity of the protein. Therefore, the Goitsuka reference meets the limitations of claims 36-69.

5b. Claims 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Goitsuka et al (April 2000) in view of the Capon et al. patent (U.S. Patent No. 5,116,964).

The disclosure of Goitsuka et al has been set forth above in paragraph 5a. However, the Goitsuka et al. reference fails to disclose that the polynucleotide (encoding human MIST protein) further comprises a heterologous nucleic acid, which is the C_H region of human immunoglobulin IgG2a to increase the half-life of the MIST protein.

Capon et al. teaches chimeric proteins for directing ligand binding partners such as growth factors, hormones or effector molecules to cells bearing ligands for the ligand binding partners comprising a ligand binding partner fused to a stable plasma protein which is capable of extending the in vivo half-life of the ligand binding partner when present as a fusion with the ligand binding partner, in particular wherein such a stable plasma protein is an immunoglobulin constant domain or albumin (see column 4, lines 57-64; column 5, lines 11-21; column 7, lines 11-27; column 8, lines 13-15).

Therefore, it would have been prima facie obvious to one having ordinary skill in the art to modify the polynucleotide of Goitsuka such that it includes a heterogenous nucleic acid sequence to obtain a chimeric protein with an increased circulating half-life, as taught by Capon et al., to obtain the known functions and advantages of the human MIST polypeptide as per the teachings of Goitsuka et al. One would have been motivated to make a chimeric nucleic acid encoding a chimeric protein comprising human MIST and human immunoglobulin to decrease its clearance rate *in vivo*. Therefore, it would have been obvious to obtain a chimeric nucleic acid encoding a chimeric protein comprising human MIST and human immunoglobulin, a long-lived molecule well known in the art as able to increase the stability of rapidly cleared molecules.

Conclusion

No claim is allowed.

Claims 36-69 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1646
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